recombinant adeno-associated virus (rAAV) vectors, compositions comprising at least two different rAAVs, host cells contacted with a composition of the invention and methods of using the vectors and compositions of the invention. In particular, Applicant discloses that two rAAV vectors each comprising different non-AAV sequences are useful to express or enhance the maintenance of sequences in the rAAVs in a cell contacted with the composition, as the rAAVs can become linked in the cell (page 6, line 26-page 7, line 8 of the specification). Thus, two or more rAAV vectors can be employed to individually deliver portions of a gene to a cell.

For example, one rAAV vector may comprise a heterologous transcriptional regulatory element, such as an enhancer, and another rAAV may comprise a minimal promoter operably linked to an open reading frame (ORF) or a portion thereof (page 6, line 26-page 7, line 8 and page 11, line 28-page 12, line 1 of the specification). Once the rAAVs are linked in a cell, the enhancer stimulates transcription of the ORF from the promoter. Alternatively, one rAAV may comprise an enhancer and a promoter while another rAAV may comprise an ORF (page 6, line 26-page 7, line 8 of the specification). Once those elements are linked in a cell, the promoter directs transcription, and the enhancer enhances transcription, of the ORF. In addition, one rAAV may comprise a promoter and at least one exon for a gene while another rAAV may comprise the remaining exons for the gene. Once those elements are linked after infection of a cell with the rAAVs, the promoter directs transcription of the exons (Figure 19). Further, one rAAV may comprise a heterologous origin of replication and may also encode protein that binds to the heterologous origin of replication while another rAAV comprises an ORF or a portion thereof (page 6, line 26-page 7, line 8 of the specification).

Based on the Applicant's disclosure and the telephonic conversation between Applicant's Representatives and the Examiner on January 14, 2002, Applicant's Representatives propose the following groups of claims for election in a revised Restriction Requirement:

claims 1-11, 24-25 and 46-47 (group A), directed to a composition comprising at least two rAAVs, in which one rAAV comprises a heterologous transcriptional regulatory element (claim 46), e.g., an enhancer (claim 8) or a promoter (claim 9), and another rAAV comprises a DNA segment other than the transcriptional regulatory element, e.g., a portion of an open reading frame (claim 4), and a host

cell contacted with such a composition;

claims 12-17 (group B), directed to a composition comprising at least two rAAVs, in which one rAAV comprises a heterologous origin of replication functional in a host cell and encodes a protein which binds to the origin of replication and another rAAV comprises at least a portion of an ORF;

claims 18, 22-23 and 44-45 (group C), directed to a rAAV vector comprising a heterologous origin of replication, a rAAV vector comprising a DNA sequence encoding a protein that binds to a heterologous origin of replication, and a plasmid comprising the vector;

claims 19-21 and 23 (group D), directed to a rAAV vector comprising at least one heterologous transcriptional regulatory element, e.g., a promoter or enhancer functional in a host cell, and a plasmid comprising the vector;

claims 26-37 and 48 (group E), directed to a method to transfer recombinant DNAs to a host cell, comprising: contacting the host cell with at least two rAAVs, in which one rAAV comprises a transcriptional regulatory element (claim 48), e.g., an enhancer (claim 32) or a promoter (claim 33), and another rAAV comprises a DNA segment other than the transcriptional regulatory element, e.g., an ORF; and

claims 38-43 (group F), directed to a method to transfer recombinant DNAs to a host cell, comprising: contacting the host cell with at least two rAAVs, in which one rAAV comprises an origin of replication and/or encodes a protein that binds to the origin of replication.

Thus, generally, the proposed restriction requirement groups together claims that are directed to compositions and host cells comprising a rAAV comprising a transcriptional regulatory element and another rAAV comprising a sequence other than the transcriptional regulatory element, or methods of using the compositions and host cells, regardless of which of the two rAAVs comprises the transcriptional regulatory element (see proposed group A which corresponds to Groups 1-4, proposed group D which corresponds to Groups 8-9, and proposed group E which corresponds to Groups 10-13). This is in contrast to the Restriction Requirement dated December 4, 2001, where for each group containing claims in which the first rAAV

comprises a particular transcriptional regulatory element there was a different group containing claims in which the second rAAV comprises the particular transcriptional regulatory element (see, for example, Group 1 and Group 4 (promoter); Group 2 and Group 3 (enhancer); Group 10 and Group 13 (promoter); and Group 11 and Group 12 (enhancer).

Also, the proposed restriction requirement groups together claims that are directed to a composition or host cell comprising at least two rAAVs in which one rAAV comprises a heterologous origin of replication and/or encodes a protein that binds to the origin of replication, or methods of employing those compositions and host cells, regardless of which rAAV comprises the origin of replication and/or encodes a protein that binds to the origin of replication (see proposed group F which corresponds to Groups 14-15).

Applicant provisionally elects, with traverse, the invention of Group 10 (claims 26-31, 33 and 48) directed to a method to transfer recombinant DNAs to a host cell, comprising: contacting the host cell with at least two rAAVs, in which the first rAAV comprises a portion of an ORF and a promoter. Reconsideration and withdrawal of the Restriction Requirement, in view of the remarks herein, is respectfully requested.

The Restriction Requirement is traversed on the basis that the inventions are so closely related within the context of the disclosure of the application that they cannot properly be considered independent and distinct within the statutory meaning of 35 U.S.C. § 121. Claims directed to a method to transfer recombinant DNAs to a host cell, comprising: contacting the host cell with at least two rAAVs, in which the first rAAV comprises a portion of an ORF and a transcriptional regulatory element which is a promoter (Group 10) are clearly related to claims directed to a method to transfer recombinant DNAs to a host cell, comprising: contacting the host cell with at least two rAAVs, in which the second rAAV comprises a transcriptional regulatory element which is a promoter and portion of an ORF (Group 13; claims 35 and 37), claims directed to a method to transfer recombinant DNAs to a host cell, comprising: contacting the host cell with at least two rAAVs, in which the first rAAV comprises a portion of an ORF and a transcriptional regulatory element which is an enhancer (Group 11; claim 32), and claims directed to a method to transfer recombinant DNAs to a host cell, comprising: contacting the host cell with at least two rAAVs, in which the second rAAV comprises a transcriptional regulatory

element which is an enhancer and portion of an ORF (Group 12; claims 34 and 36).

The Restriction Requirement is also traversed on the basis that Restriction Requirements are optional in all cases. M.P.E.P. § 803. If the search and examination of an entire application can be made without serious burden, the Examiner must examine it on the merits, even though it arguably may include claims to distinct or independent inventions. M.P.E.P. § 803. Moreover, it is submitted that Applicant should not be required to incur the additional costs associated with the filing of multiple divisional applications in order to obtain protection for the claimed subject matter. Due to the relatedness of the subject matter of the claims in Groups 10-13, the claims in Groups 10-13, can be efficiently and effectively searched in a single search with no additional burden placed on the Examiner. Evidence that the claims in at least Groups 10-13 can be efficiently and effectively searched in a single search with no additional burden placed on the Examiner is provided in the Restriction Requirement as those claims are in the same class and subclass (class 930 and subclass 33) for search purposes.

Further, as claim 48 is a linking claim for claims in Groups 10-13, claims 26-37 and 48 should be examined in the same application. M.P.E.P. 809.03.

Thus, the Restriction Requirement is properly traversed. Accordingly, reconsideration and withdrawal of the Restriction Requirement is respectfully requested.

The Examiner is invited to contact Applicant's Representatives at the number given below if there are any questions regarding this Response or if prosecution of this application may be assisted thereby.

Respectfully submitted,

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner of Patents, Washington, D.C. 20231, on this 4th day of June, 2002.

Candis B. Buending
Name

Signature